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Sex differential in COVID-19 mortality varies markedly by age

In the COVID-19 pandemic, we have emphasised the importance for epidemiological data to be presented by age and sex groups.^{1,2} This call has also been made by the European Association of Science Editors³ and The Lancet.⁴ Without these data, the public are unable to make truly informed choices about their own disease risk, and public policy responses cannot be specifically targeted.

The prevailing view is that although the number of male cases is not dissimilar to the number of female cases, men have about twice the risk of death from COVID-19, leading to a range of hypotheses, from lifestyles to differences in chromosomal structure.^{5–7} Although graphs describing disaggregated national statistical data can be found on the Global Health 50/50 website,⁸ the underlying data are not shown and, to the best of our knowledge, have not been described in the literature.

We examined the sex ratio through the life course to see if the COVID-19 mortality sex-differential was the same at every age. We analysed data collated by the National Institute for Demographic Studies from national statistical agencies across England and Wales, France, Germany, Italy, Netherlands, Portugal, Korea, and Spain, covering an estimated population of 194 349 591 men and 201 715 364 women from the beginning of the pandemic until June 21, 2020.⁹ Belgium and USA were not included due to presentation of data in different age categories.

77 652 men died and 59 591 women died. The overall male to female mortality sex ratio per 100 000 population was 1·4 (crude ratio 1·3). This ratio was not equal at all ages. For example, for people aged 0–9 years the ratio was 0·81. The ratio was 1·9 in the 40–49 years age group, 2·3 in the 50–59 year age group, 2·6 in the 60–69 years age group, and 1·65 in people older than 80 years (appendix p 1).

There was some variation across countries, although broadly the pattern was similar, and the numbers became too small for clear-cut interpretation (appendix p 3).

These data alter our understanding of male–female differences; the relationship is not straightforward, and efforts should now be made to understand risk based on the interaction of sex and age, along with other factors.

Hypotheses based on risk factors that are known to change with both sex and age seem to be the most probable explanations for the differences observed. These include differences in occupation, lifestyle (including smoking and alcohol use), medical comorbidities, or use of medications. These explanations reflect social and cultural factors related to gender rather than the biology of sex. Genetic explanations will need to consider the interaction of age, sex, and the risk factors previously mentioned through the life course, including gene expression and epigenetics.

Disaggregated data allow public health authorities to tailor mortality prevention strategies to prioritise those most at risk. Although we are developing indirect standardisation methods,¹⁰ we urge nations to supply age and sex specific data, not only for an accurate description of the pandemic, but also for the calculation of directly standardised rates internationally—something WHO cannot do globally for lack of comprehensive sex and age group specific data.

We declare no competing interests.

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Table 1: in 10 year age bands by sex, population, deaths, mortality per 100,000, risk ratio in England & Wales, France, Germany, Italy, Netherlands, Portugal, Korea and Spain

Age group	Population		Deaths		Deaths per 100,000		Sex ratio (M:F)
	Male	Female	Male	Female	Male	Female	
0-9	19923780	18935073	6	7	0.03	0.04	0.81
10-19	21333098	20087329	14	9	0.07	0.04	1.46
20-29	23719884	22435304	94	50	0.40	0.22	1.78
30-39	25310993	25157644	282	170	1.11	0.68	1.65
40-49	27912903	27945866	993	531	3.56	1.90	1.87
50-59	29327752	29834735	3776	1661	12.9	5.57	2.31
60-69	22611177	24271853	9590	4024	42.4	16.6	2.56
70-79	15668774	18552985	21830	10940	139.3	59.0	2.36
80+	8541230	14494575	41067	42199	480.8	291.1	1.65
ALL	194349591	201715364	77652	59591	40.0	29.5	1.35

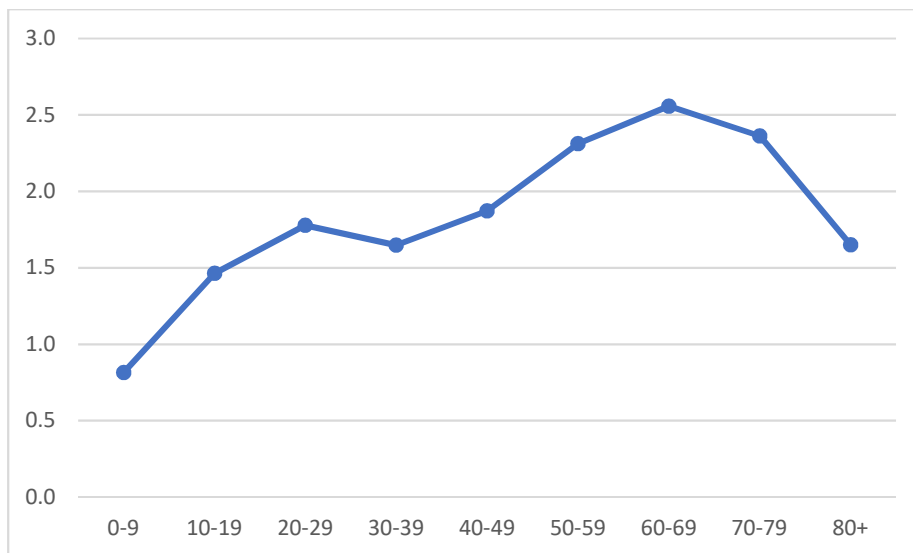


Figure 1: Mortality sex ratio per 100,000 population across England & Wales, France, Germany, Italy, Netherlands, Portugal, Korea and Spain

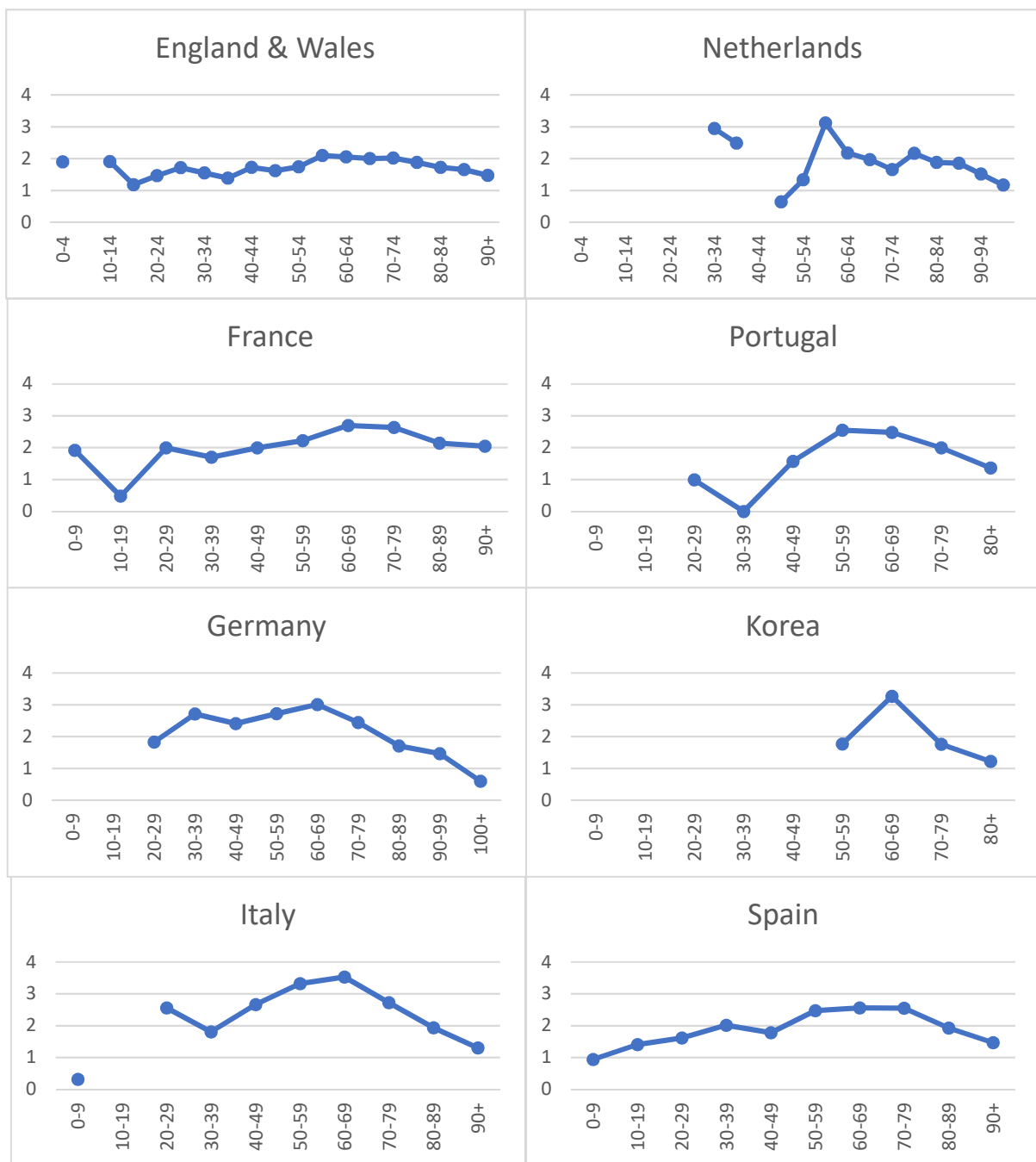


Figure 2: Mortality sex ratio per 100,000 population in England & Wales, France, Germany, Italy, Netherlands, Portugal, Korea and Spain